Refine Search

Search Results -

Term	Documents
"40"	705895
40S	1234
MG	151794
MGS	1871
"50"	700848
50S	970
(7 AND (("40" ADJ MG) OR ("50" ADJ MG))).PGPB.	60
(L7 AND (40 ADJ MG OR 50 ADJ MG)).PGPB.	60

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L10

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Saturday, September 23, 2006 Purge Queries | Printable Copy | Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB; PLUR=YES; OP=ADJ			
L10	L7 and (40 adj mg or 50 adj mg)	60	L10
DB=USPT; PLUR=YES; OP=ADJ			
L9	L7	85	L9
DB=EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L8	L7	1	L8

DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ

L7	L6 and (graft$ or transplant$ or toleran$)	191	L7
L6	(cd4 or cd8)same (40 or 50)same (mg)same(antibod$ or immunoglobulin$)	242	L6
L5	(l1 or L2 or l3) and (cd4 or cd8)	14	L5
L4	ringler douglas.in.	17	L4
L3	ringler douglas? .in.	0	L3
L2	rao patricia.in.	22	L2
L1	winsor-hines.in.	11	L1

END OF SEARCH HISTORY

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Set     Items   Description
S1         31   E2-E4
S2         13   E1-E4
S3         21   E1-E5
S4         19   (S1 OR S2 OR S3) AND (CD8 OR CD4)
S5         16   RD S4  (unique items)
S6          2   S5 AND 40
S7          2   RD S6  (unique items)
S8         14   (CD8)(10N)(ANTIBOD? OR IMMUNOGLOBULIN?) AND (CD4)(10N)(ANT-
              IBOD? OR IMMUNOGLOBULIN?) AND 40(W)MG
S9          8   RD S8  (unique items)
S10        34   ((CD8)(10N)(ANTIBOD? OR IMMUNOGLOBULIN?) OR (CD4)(10N)(ANT-
              IBOD? OR IMMUNOGLOBULIN?)) AND 40(W)MG
S11        16   RD S10  (unique items)
S12       126   (ANTIBOD? OR IMMUNOGLOBULIN?)(10N) (40(W)MG OR 50(W)MG) AND
              (TRANSPLANT? OR GRAFT? OR TOLERAN?)
S13       106   RD S12  (unique items)
S14        91   S13 AND PY<2002
S15      1474   HIGH(10N)(DOSE? OR DOSING)(20N)(ANTIBOD?)(20N)(TRANSPLANT?
              OR GRAFT? OR TOLERAN?)
S16       400   S15 AND TOLERAN?
S17       292   S16 AND PY<2002
S18       175   S17 AND PY>1990
S19       100   RD S18  (unique items)
S20      5197   TOLERAN? AND IMMUNOL? AND (TRANSPLANT? OR GRAFT?) AND REVI-
              EW?
S21       195   TOLERAN?(20N)(DIFFICUL? OR CORRELAT? OR PREDICT? OR LACK OR
              GRAIL) AND IMMUNOL? AND (TRANSPLANT? OR GRAFT?) AND REVIEW?
S22        29   RD S1  (unique items)
S23       175   RD S21  (unique items)
S24       161   S23 AND PY>1990
?
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s14/7/1,2,7,29,31,34,88

14/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013780337 BIOSIS NO.: 200200373848
Safety, pharmacokinetics and pharmacodynamics of recombinant human tumour necrosis factor-binding protein-1 (Onercept) injected by intravenous, intramuscular and subcutaneous routes into healthy volunteers
AUTHOR: Trinchard-Lugan I (Reprint); Ho-Nguyen Q; Bilham W M; Buraglio M; Ythier A; Munafo A
AUTHOR ADDRESS: Serono International SA, 12, Chemin des Aulx, 1228, Plan-les-Ouates, Geneva, Switzerland**Switzerland
JOURNAL: European Cytokine Network 12 (3): p391-398 July-Sept., 2001
2001
MEDIUM: print
ISSN: 1148-5493
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The safety, pharmacokinetics and pharmacodynamics of recombinant human tumour necrosis factor-binding protein-1 (r-hTBP-1, Onercept) were investigated after intravascular and extravascular injection, in three studies in healthy volunteers. Subjects received Onercept as single intravenous doses of 5, 15, 50 and 150 mg, or single IV, IM, SC injection of 50 mg, or six repeated SC injections of ***50*** ***mg*** . Based on vital signs, hematology and blood chemistry, antibodies to study drug and local tolerability, r-hTBP-1 exhibited a remarkably safe profile. There was no evidence of alteration of hepatic oxidative metabolism. Recombinant-hTBP-1 showed linear pharmacokinetics that could be described by a triexponential model, and exhibited an initial half-life of 30 min, an intermediate half-life of 4 hours and a terminal elimination half-life of about 15 hours, although it was prolonged to 21 hours after repeated SC injections. The total clearance was estimated at 4 l/h. The initial (Vc) and steady state (Vss) volumes of distribution were approximately 4 l and 10 l, respectively. Renal clearance was minimal, representing around 2.5% of the total clearance, and remained constant after increasing doses of r-hTBP-1. The absorption was slow and biphasic. The immunoactivity of r-hTBP-1 was closely related to its biological activity, although the assessment was limited to only some of the samples. As anticipated in normal healthy volunteers, the pharmacodynamic response was generally not different from placebo. Total TNF-alpha serum levels increased slightly, 1 hour following IV administration of 50 mg and 150 mg r-hTBP-1. However, no major increase in the active entity levels (free TNF-alpha) was observed. In addition, no TNF-alpha-driven biological response was observed, i.e. C-reactive protein, IL-6 and fibrinogen remained almost constant, as did transferrin and albumin. Its safety profile and pharmacokinetic characteristics make Onercept a candidate drug suitable for antagonising pathologically high levels of TNF-alpha as reported in inflammatory, immune and cardiovascular diseases.

14/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013121044 BIOSIS NO.: 200100292883
Adenovirus infections in haematopoetic stem cell transplant recipients: Is there a role for immunotherapy?

AUTHOR: Chakrabarti Suparno (Reprint); Collingham Kathryn E (Reprint); Pillay Deenan (Reprint); Fegan Christopher D (Reprint); Milligan Donald W (Reprint)
AUTHOR ADDRESS: Haematology and Public Health Laboratories, Heartlands Hospital, Birmingham, West Midlands, UK**UK
JOURNAL: Blood 96 (11 Part 1): p191a November 16, 2000 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000; 20001201
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In a prospective surveillance study of adenovirus infections in stem cell transplant recipients, we examined samples of stool, urine and throat weekly by electron microscopy and culture (MKC, MRC5 and PLC cell line) from the start of conditioning treatment to 6 months post- ***transplant*** . PCR assay was performed on whole blood using hexon-based primers when a positive culture was obtained. 100 patients (50 allo; 50 auto) with a median age of 36 years (17-51) were evaluated. At a median follow-up of 12 months (1-30), adenovirus was isolated from 11/50 allograft (22%) and 0/50 autograft recipients. Adenovirus was isolated from stool in all infected patients at a median of 105 days (15-202). Other sites of virus isolation were urine (2), throat (1) and blood PCR (2). All isolates were serotyped as adenovirus type 2. The median duration of asymptomatic excretion was 2 weeks (2-14 weeks). 4 patients (36%) developed symptom:- hepatitis 2, colitis 1, pneumonia (multiple pathogens) 1; three of them (27%) failed ribavirin therapy and died from the infection. Adenovirus infection was diagnosed in 0/12 unmanipulated transplants and 11/38 (28%) of T cell depleted ***transplants*** (p=0.04). The highest incidence was in recipients of nonmyeloablative ***transplants*** :- 7/14 (50%), p=0.006, OR 8.0 (CI 1.8-35). There was also a correlation with the dose of Campath (anti-CD52) antibody with only 2 infections in 28 patients receiving 0-50 mg of Campath versus 9/23 in patients receiving > ***50*** ***mg*** of the ***antibody*** ; p=0.01, OR=8.1 (CI 1.5-42). Adenovirus disease correlated with the absolute lymphocyte count at the onset of the infection which was 151+-129/mm3 in patients developing adenovirus disease, compared with 514+-452/mm3 in patients not developing symptomatic disease (p=0.02). All 3 patients who required continued immunosuppressive therapy developed adenovirus disease and had a fatal outcome, whereas all the patients who were off immunosuppression at the time of virus isolation(n=6) or received donor lymphocytes (n=2) cleared the virus (p=0.006). Also both patients with a positive blood PCR died, whereas none of the 7 patients with a negative PCR succumbed (p=0.02). In this study adenovirus infection was related to the intensity of immunosuppression in the conditioning and the development of adenovirus disease correlated with the lymphocyte count at the time of virus isolation. The outcome was significantly improved in patients who had immunosuppression withdrawn or received donor lymphocyte infusion.

14/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007108379 BIOSIS NO.: 199089026270
IMMUNOREGULATORY EFFECT OF ANTIBODY ON DELAYED-TYPE HYPERSENSITIVITY IN MICE
AUTHOR: MORIKAWA Y (Reprint); KURIBAYASHI K; SAITO K

AUTHOR ADDRESS: DEP PATHOL, WAKAYAMA MED SCH, 9-BANCHO 27, WAKAYAMA CITY, WAKAYAMA 640, JPN**JAPAN
JOURNAL: International Archives of Allergy and Applied Immunology 90 (2): p130-136 1989
ISSN: 0020-5915
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We analyzed the conditions for in vivo toleration of delayed-type hypersensitivity (DTH). The intravenous injection of a high dose of keyhole-limpet hemocyanin (KLH) into BALB/c mice did not induce DTH in vivo, but the serum titers of the anti-KLH antibody were significantly elevated. This lack of DTH response was antigen-specific, and the intravenous injection of the antigen induced effector-phase suppressor T cells. The findings suggested that the lack of a DTH response brought about by the intravenous injection of a high dose of antigen was not immunological ***tolerance*** . Treatment with a high dose (250 mg/kg) of cyclophosphamide.sbd.but not a low dose (***50*** ***mg*** /kg).sbd.enhanced the DTH, but suppressed ***antibody*** production. These results indicate that humoral immune responses participate in the regulation of DTH. In addition, the transfer of serum or immunoglobulin from mice that were injected intravenously with a high dose of the antigen suppressed the DTH. We concluded that the antibodies regulate DTH in the antigen-specific manner.

14/7/29 (Item 22 from file: 73)
DIALOG(R)File 73:EMBASE

05559418 EMBASE No: 1993327518
A successful regimen to reduce cytomegalovirus disease in heart transplant patients

Jazzar A.; Cooper D.K.C.; Muchmore J.S.; Pribil A.; Chaffin J.S.; Zuhdi N.
Oklahoma Transplantation Institute, Baptist Medical Center, 3300 NW Expressway,Oklahoma City, OK 73112 United States
Transplantology: Journal of Cell and Organ Transplantation (TRANSPLANT. J. CELL ORGAN TRANSPLANT.) (Spain) 1993, 4/2 (47-53)
CODEN: TANSE
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH; SPANISH

Between January 1987 and June 1988, 57 patients underwent heart ***transplantation*** (group 1: follow-up 6-36 months: mean 17.3 months). Immunosuppressive therapy consisted of cyclosporine (CsA), azathioprine (AZA), and low-dose steroids, plus prophylactic antilymphoblast globulin (ALG). Twenty-two patients (39%) developed clinically significant, proven cytomegalovirus (CMV) disease. All received monotherapy with intravenous ganciclovir. Six had concomitant pulmonary infections with other organisms, 4 of which were due to Pneumocystis carinii (PC). Overall mortality was 18%, possibly directly related to CMV infection in one case. Between July 1989 and October 1991 inclusive, 50 patients underwent heart ***transplantation*** (group 2: follow-up 3-31 months; mean 15.8 months). Immunosuppressive therapy consisted of CsA, AZA and high-dose steroids, with no ALG. CMV prophylaxis was given to every patient in the form of oral acyclovir for 3 months (at approximately 50 mg/kg/day) and commercially available ***immunoglobulin*** (500 mg/kg i.v. on days 7 and 35). Prophylaxis against PC was by trimethoprim/sulfamethoxazole (1 double-strength tablet/day) indefinitely. Only 2 patients (4%) in group 2 developed CMV disease ($p < 0.001$ vs group 1); none developed PC infection.

Overall mortality was 4% (p < 0.03 vs group 1), possibly associated with CMV infection in one case. The incidence of acute rejection requiring extra therapy in the first 3-month period was 0.47 episodes/patient in group 1 and 0.24 episodes/patient in group 2 (p < 0.01). We conclude that CMV (and PC) infections can be largely prevented in heart transplant recipients.

14/7/31 (Item 24 from file: 73)
DIALOG(R)File 73:EMBASE

05536121 EMBASE No: 1993304220
Chimeric CD4 monoclonal antibody cM-T412 as a therapeutic approach to rheumatoid arthritis
Van der Lubbe P.A.; Reiter C.; Breedveld F.C.; Kruger K.; Schattenkirchner M.; Sanders M.E.; Riethmuller G.
Department of Rheumatology, Building 1, University Hospital, P.O. Box 9600,2300 RC Leiden Netherlands
Arthritis and Rheumatism (ARTHRITIS RHEUM.) (United States) 1993, 36/10 (1375-1379)
CODEN: ARHEA ISSN: 0004-3591
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Objective. To investigate the effects of chimeric CD4 monoclonal antibody cM-T412 treatment in patients with rheumatoid arthritis (RA). Methods. Thirty-two RA patients received daily doses of 10, 50, or 100 mg of cM-T412 intravenously for 7 days. Results. There was a sustained decrease in the number of CD4+ T lymphocytes in all patients. Those who received ***50*** mg and 100 mg of the antibody experienced significant reductions in disease activity. Conclusion. Treatment with cM-T412 appears to have a dose-dependent beneficial effect in RA patients. The clinical effects of cM-T412 are independent of the depressed numbers of circulating CD4+ T cells.

14/7/34 (Item 27 from file: 73)
DIALOG(R)File 73:EMBASE

05112186 EMBASE No: 1992252402
Treatment of rheumatoid arthritis with single dose or weekly pulses of chimaeric anti-CD4 monoclonal antibody
Choy E.H.S.; Chikanza I.C.; Kingsley G.H.; Corrigall V.; Panayi G.S.
Rheumatology Unit, Guy's Hospital, St Thomas Street,London SE1 9RT United Kingdom
Scandinavian Journal of Immunology (SCAND. J. IMMUNOL.) (United Kingdom) 1992, 36/2 (291-298)
CODEN: SJIMA ISSN: 0300-9475
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The aetiology of rheumatoid arthritis is unknown but CD4sup + T cells are known to be involved in its pathogenesis. Because of this, anti-CD4 monoclonal antibody has been used in open studies with clinical benefit in up to 60% of patients. We have used a chimaeric anti-CD4 monoclonal antibody (cM-T412, Centocor) in a randomized, double-blinded, placebo controlled trial as treatment for rheumatoid arthritis. Nine patients with active rheumatoid arthritis resistant to traditional disease-modifying drugs were recruited. Four received an intravenous ***50*** ***mg*** bolus of antibody, and three received 50 mg weekly for four

consecutive weeks. Two patients received placebo. Despite a marked reduction (P < 0.001) in peripheral blood CD4sup + lymphocytes, there was no significant clinical improvement in any of these patients. The decrease in CD4sup + lymphocyte number lasted one week after a single 50 mg dose of cM-T412 but was more prolonged in the patients who received four infusions. CD8sup + T cells, CD16sup + cytotoxic cells and CD14sup + monocytes showed only a transient reduction. It may be concluded thatthe therapeutic efficacy of anti-CD4 therapy is not directly related to CD4sup + T-cell lymphopenia.

14/7/88 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08717451 PMID: 2088961
Fetal pancreas ***transplantation*** in non-obese diabetic (NOD) mice. A comparison of iso-, allo- and xenografts.
Mandel T E; Koulmanda M; Bacelj A
Walter and Eliza Hall Institute of Medical Research, Parkville, Australia.
Hormone and metabolic research. Supplement series (GERMANY) ***1990***, 25 p166-73, ISSN 0170-5903--Print Journal Code: 0330417
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Prediabetic NOD/Wehi male mice aged 100 days were each transplanted under the renal capsule with three pieces of organ-cultured fetal pancreas; an isograft of NOD pancreas, an allograft of CBA (H-2k) pancreas, and a xenograft of fetal pig tissue. Groups of mice were given immunosuppression on days -1, 0 and +1 relative to transplantation with either an anti-CD4 monoclonal ***antibody*** (MAb, GK1.5), with or without a low dose (50 mg /kg IP) of cyclosporin A (CsA), with CsA alone or phosphate buffered saline in non-immunosuppressed controls. Flow cytometric analysis showed that CD4+ cells were severely depleted in mice that had been given GK1.5 11 days previously, but these cells slowly recovered to 35% of control levels by day 28, and 70% by day 56. The xenografted islets were slowly destroyed in the MAb-treated mice, at a rate which was slower than rejection of the allografts. At 28 days, when the allografts were severely affected, the xenografts were generally well preserved. The immunosuppression also did not stop mononuclear cell infiltration of the isografts. However, by 56 days all xenografts and most allografts were totally destroyed, and the isografts were infiltrated to an extent similar to that present in the pancreas. These results suggest that xenogeneic islets are no more and possibly even less immunogeneic than MHC-mismatched allografts, and are only slowly rejected after a peri-transplant period of immunosuppression used to transiently deplete CD4+ cells. However, the transient immunisuppression used did not result in indefinite xenograft survival suggestive of immunological ***tolerance*** .
Record Date Created: 19910524
Record Date Completed: 19910524
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Set	Items	Description
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S2	13	E1-E4
S3	21	E1-E5
S4	19	(S1 OR S2 OR S3) AND (CD8 OR CD4)
S5	16	RD S4 (unique items)
S6	2	S5 AND 40

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S7          2   RD S6  (unique items)
S8         14   (CD8)(10N)(ANTIBOD? OR IMMUNOGLOBULIN?) AND (CD4)(10N)(ANT-
               IBOD? OR IMMUNOGLOBULIN?) AND 40(W)MG
S9          8   RD S8  (unique items)
S10        34   ((CD8)(10N)(ANTIBOD? OR IMMUNOGLOBULIN?) OR (CD4)(10N)(ANT-
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S11        16   RD S10  (unique items)
S12       126   (ANTIBOD? OR IMMUNOGLOBULIN?)(10N) (40(W)MG OR 50(W)MG) AND
               (TRANSPLANT? OR GRAFT? OR TOLERAN?)
S13       106   RD S12  (unique items)
S14        91   S13 AND PY<2002
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     $0.44  Estimated total session cost   0.221 DialUnits

SYSTEM:OS  - DIALOG OneSearch
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         (c) 2006 The Thomson Corporation
  File  73:EMBASE 1974-2006/Sep 22
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  File 155:MEDLINE(R) 1950-2006/Sep 25
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  File 399:CA SEARCH(R) 1967-2006/UD=14513
         (c) 2006 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.

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E2        4  AU=RINGLER DOUGLAS
E3        0 *AU=RINGLER DOUGLAS ?
E4       27  AU=RINGLER DOUGLAS J
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E9        1  AU=RINGLER F.
E10       2  AU=RINGLER G
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E12       2  AU=RINGLER G.

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             27  AU=RINGLER DOUGLAS J
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? e au=winsor-hines dawn ?

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E4        6  AU=WINSOR-HINES, DAWN
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E7       22  AU=WINSOR, BARBARA
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E9        1  AU=WINSOR, C. E.
E10       1  AU=WINSOR, CLAIRE
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Ref    Items  Index-term
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E14        1  AU=WINSOR, D. L.
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E19        2  AU=WINSOR, DONALD K.
E20        1  AU=WINSOR, DONALD KEITH, JR.
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E22        1  AU=WINSOR, ELIZABETH
E23        1  AU=WINSOR, ELSA L.
E24        2  AU=WINSOR, F. J.

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                4  AU=WINSOR-HINES DAWN
                0  AU=WINSOR-HINES DAWN ?
                6  AU=WINSOR-HINES, DAWN
      S2       13  E1-E4
? e au=rao patricia ?

Ref    Items  Index-term
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E8         1  AU=RAO PAUL
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E10        2  AU=RAO PAUL S K
E11        2  AU=RAO PAVITRA N
E12        4  AU=RAO PAWAN K

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? s e1-e5
                1  AU=RAO PATCHALA J R MOHAN
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               13  AU=RAO PATRICIA E
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               13  S2
               21  S3
           145743  CD8
           238007  CD4
      S4       19  (S1 OR S2 OR S3) AND (CD8 OR CD4)
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? s s5 and 40
               16  S5
          1345499  40
      S6        2  S5 AND 40
? rd s6
      S7        2  RD S6  (unique items)
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? t s7/3/all

7/3/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015320175 BIOSIS NO.: 200510014675
Induction of immunological tolerance/hyporesponsiveness in baboons with a nondepleting CD4 antibody
AUTHOR: Winsor-Hines Dawn; Merrill Christopher; O'Mahony Mark; Rao Patricia E; Cobbold Stephen P; Waldmann Herman; Ringler Douglas J; Ponath Paul D (Reprint)
AUTHOR ADDRESS: TolerRx Inc, 300 Technol Sq, Boston, MA 02130 USA**USA
AUTHOR E-MAIL ADDRESS: pponath@tolerrx.com
JOURNAL: Journal of Immunology 173 (7): p4715-4723 OCT 1 04 2004
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

7/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009611558 BIOSIS NO.: 199598079391
Macrophage function in simian AIDS. Killing defects in vivo are independent of macrophage infection associated with alterations in Th phenotype, and reversible with IFN-gamma
AUTHOR: Brodie Scott J (Reprint); Sasseville Vito G; Reimann Keith A; Simon Meredith A; Sehgal Prabhat K; Ringler Douglas J
AUTHOR ADDRESS: Harvard Med. School, New Enland Reg. Primate Res. Cent., P.O. Box 9102, Southborough, MA 01772-9102, USA**USA
JOURNAL: Journal of Immunology 153 (12): p5790-5801 1994 1994
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
? t s5/3/all

5/3/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015320175 BIOSIS NO.: 200510014675
Induction of immunological tolerance/hyporesponsiveness in baboons with a nondepleting CD4 antibody
AUTHOR: Winsor-Hines Dawn; Merrill Christopher; O'Mahony Mark; Rao Patricia E; Cobbold Stephen P; Waldmann Herman; Ringler Douglas J; Ponath Paul D (Reprint)
AUTHOR ADDRESS: TolerRx Inc, 300 Technol Sq, Boston, MA 02130 USA**USA
AUTHOR E-MAIL ADDRESS: pponath@tolerrx.com
JOURNAL: Journal of Immunology 173 (7): p4715-4723 OCT 1 04 2004
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015256293 BIOSIS NO.: 200500162465
Differentiation and expression of T cells with regulatory function from human peripheral lymphocytes by stimulation in the presence of TGF-beta.
AUTHOR: Rao Patricia E (Reprint); Petrone Andria L; Ponath Paul A
AUTHOR ADDRESS: TolerRx, 300 Technol Sq, Cambridge, MA, 02139, USA**USA
AUTHOR E-MAIL ADDRESS: dandp77@earthlink.net
JOURNAL: Journal of Immunology 174 (3): p1446-1455 February 1, 2005 2005
MEDIUM: print
ISSN: 0022-1767 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011561255 BIOSIS NO.: 199800355502
Increased expression of alpha4beta7 integrin on food allergen-stimulated CD4+ T cells in active food allergic enterocolitis
AUTHOR: Kohno Yoichi (Reprint); Shimojo Naoki; Aoyagi Masahiko; Sannomiya Yoshio; Nishimuta Toshiyuki; Kojima Hiroyuki; Katsuki Toshiyuki; Tomiita Minako; Lazarovits Andrew I; Ringler Douglas; Niimi Hiroo
AUTHOR ADDRESS: Dep. Pediatr., Chiba Univ. Sch. Med., 1-8-1 Inohana, Chuo-ku, Chiba 260-8670, Japan**Japan
JOURNAL: Allergology International 47 (2): p99-102 June, 1998 1998
MEDIUM: print
ISSN: 1323-8930
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009767795 BIOSIS NO.: 199598235628
Cross-Linking of CD4 in a TCR/CD3-Juxtaposed Inhibitory State: A pFRET Study
AUTHOR: Szabo Gabor Jr (Reprint); Weaver James L; Pine P Scott; Rao Patricia E; Aszalos Adorjan
AUTHOR ADDRESS: Dep. Biophysics, Univ. Med. Sch. Debrecen, 4012 Debrecen, Nagyerdei krt 98, Hungary**Hungary
JOURNAL: Biophysical Journal 68 (3): p1170-1176 1995 1995
ISSN: 0006-3495
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009611558 BIOSIS NO.: 199598079391
Macrophage function in simian AIDS. Killing defects in vivo are independent of macrophage infection associated with alterations in Th phenotype, and reversible with IFN-gamma
AUTHOR: Brodie Scott J (Reprint); Sasseville Vito G; Reimann Keith A; Simon

Meredith A; Sehgal Prabhat K; Ringler Douglas J
AUTHOR ADDRESS: Harvard Med. School, New Enland Reg. Primate Res. Cent., P.O. Box 9102, Southborough, MA 01772-9102, USA**USA
JOURNAL: Journal of Immunology 153 (12): p5790-5801 1994 1994
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009475204 BIOSIS NO.: 199497496489
Artifactual staining of monoclonal antibodies in two-color combinations is due to an immunoglobulin in the serum and plasma
AUTHOR: Nicholson Janet K A (Reprint); Rao Patricia E; Calvelli Theresa; Stetler-Stevenson Maryalice; Browning Sandra W; Yeung Lily; Marti Gerald E
AUTHOR ADDRESS: 1-1202, 1600 Clifton Rd. NE, Centers Dis. Control, Atlanta, GA 30333, USA**USA
JOURNAL: Cytometry 18 (3): p140-146 1994 1994
ISSN: 0196-4763
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009429571 BIOSIS NO.: 199497450856
Cytochalasin D modulates CD4 crosslinking sensitive mitogenic signal in T lymphocytes
AUTHOR: Aszalos Adorjan (Reprint); Pine P Scott (Reprint); Weaver James L (Reprint); Rao Patricia E
AUTHOR ADDRESS: Cent. Drug Evaluations and Res., FDA, 200 C St. S.W., Washington, DC 20204, USA**USA
JOURNAL: Cellular Immunology 157 (1): p81-91 1994 1994
ISSN: 0008-8749
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008991627 BIOSIS NO.: 199497012912
Analysis of simian immunodeficiency virus sequence variation in tissue of rhesus macaques with simian AIDS
AUTHOR: Kodama Toshiaki (Reprint); Mori Kazuyasu; Kawahara Takashi; Ringler Douglas J; Desrosiers Ronald C
AUTHOR ADDRESS: Div. Primate Med., Oregon Primate Res. Center, Med. Res. Foundation Oregon, 505 NW 185th Ave., Beaverton, OR 97006, USA**USA
JOURNAL: Journal of Virology 67 (11): p6522-6534 1993 1993
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract

LANGUAGE: English

5/3/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008911323 BIOSIS NO.: 199396075739
An immunohistologic study of granulomatous inflammation in SIV-infected rhesus monkeys
AUTHOR: Horvath Christopher J; Hunt Ronald D; Simon Meredith A; Sehgal Prabhat K; Ringler Douglas J (Reprint)
AUTHOR ADDRESS: Div. Comparative Pathol., Harvard Med. Sch., New England Regional Primate Res. Cent., Southborough, MA 01772-9102, USA**USA
JOURNAL: Journal of Leukocyte Biology 53 (5): p532-540 1993
ISSN: 0741-5400
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008847609 BIOSIS NO.: 199396012025
Restricted replication of simian immunodeficiency virus strain 239 in macrophages is determined by env but is not due to restricted entry
AUTHOR: Mori Kazuyasu; Ringler Douglas J; Desrosiers Ronald C (Reprint)
AUTHOR ADDRESS: Dep. Microbiol., New England Regional Primate Res. Center, Harvard Med. Sch., One Pine Hill Drive, Box 9102, Southborough, MA 01722-9102, USA**USA
JOURNAL: Journal of Virology 67 (5): p2807-2814 1993
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008748409 BIOSIS NO.: 199395050675
CD4 changes conformation upon ligand binding
AUTHOR: Szabo Gabor Jr; Pine P Scott; Weaver James L; Rao Patricia E; Aszalos Adorjan (Reprint)
AUTHOR ADDRESS: Cent. Drug Evaluation Res., FDA, 200 C St., Washington, D.C. 20204, USA**USA
JOURNAL: Journal of Immunology 149 (11): p3596-3604 1992
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008725848 BIOSIS NO.: 199395028114

Direct involvement of the CDR3-like domain of CD4 in T helper cell activation
AUTHOR: McDonnell James M; Blank Kenneth J; Rao Patricia E; Jameson Bradford A (Reprint)
AUTHOR ADDRESS: Jefferson Cancer Inst., Thomas Jefferson University, 802 Bluemle Life Sci., 233 S. 10th St., Philadelphia, Pa. 19107, USA**USA
JOURNAL: Journal of Immunology 149 (5): p1626-1630 1992
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/13 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15301700 PMID: 15661903
Differentiation and expansion of T cells with regulatory function from human peripheral lymphocytes by stimulation in the presence of TGF-{beta}.
Rao Patricia E; Petrone Andria L; Ponath Paul D
TolerRx, Cambridge, MA 02139, USA. dandp77@earthlink.net
Journal of immunology (Baltimore, Md. - 1950) (United States) Feb 1 2005, 174 (3) p1446-55, ISSN 0022-1767--Print Journal Code: 2985117R
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

5/3/14 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

144106620 CA: 144(7)106620j PATENT
Humanized anti-CD4 and anti-CD8 antibodies with reduced Fc receptor and complement binding for inducing immune tolerance to antigen or autoantigen and preventing transplant rejection
INVENTOR(AUTHOR): Winsor-Hines, Dawn; Rao, Patricia; Ringler, Douglas, J., V.; Ponath, Paul
LOCATION: USA
ASSIGNEE: Tolerrx, Inc.
PATENT: PCT International ; WO 200602377 A2 DATE: 20060105
APPLICATION: WO 2005US22500 (20050621) *US 2004PV582181 (20040622)
PAGES: 165 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:

IPCR/8 + Level	Value	Position	Status	Version	Action	Source	Office:
C07K-0016/28	A	I	F	B	20060101	H	EP
A61K-0039/395	A	I	L	B	20060101	H	EP

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BW; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; EG; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KM; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NA; NG; NI; NO; NZ; OM; PG; PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; SM; SY; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW DESIGNATED REGIONAL: AT; BE; BG; CH ; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IS; IT; LT; LU; MC; NL; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG; BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ; TZ; UG; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

5/3/15 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2006 American Chemical Society. All rts. reserv.

140004071 CA: 140(1)4071f PATENT
Humanized anti-CD4 antibodies for tolerizing primates to therapeutic antigen, protein, peptide, cell or gene therapy agent
INVENTOR(AUTHOR): Frewin, Mark; Waldmann, Herman; Gorman, Scott; Hale, Geoff; Rao, Patricia; Kornaga, Tadeusz; Ringler, Douglas; Cobbold, Stephen; Winsor-Hines, Dawn
LOCATION: UK,
PATENT: U.S. Pat. Appl. Publ. ; US 20030219403 A1 DATE: 20031127
APPLICATION: US 353708 (20030129) *GB 200114517 (20010614) *GB 200122724 (20010920) *US PV345194 (20011019) *US PV373470 (20020418) *US PV373471 (20020418) *US 171452 (20020613)
PAGES: 45 pp., Cont.-in-part of U.S. Ser. No. 171,452. CODEN: USXXCO
LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: 424085200; A61K-038/20A; A61K-039/395B

5/3/16 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2006 American Chemical Society. All rts. reserv.

138054547 CA: 138(5)54547v PATENT
TRX1 antibodies for inducing immune tolerance and treating organ graft rejection
INVENTOR(AUTHOR): Frewin, Mark; Waldmann, Herman; Gorman, Scott; Hale, Geoff; Rao, Patricia; Kornaga, Tadeusz; Ringler, Douglas; Cobbold, Stephen; Winsor-Hines, Dawn
LOCATION: UK,
ASSIGNEE: Isis Innovation Limited; Cambridge University Technical Services Limited; Tolerrx Inc.
PATENT: PCT International ; WO 2002102853 A2 DATE: 20021227
APPLICATION: WO 2002GB2796 (20020614) *GB 200114517 (20010614) *GB 200122724 (20010920) *US PV345194 (20011019) *US PV373470 (20020418) *US PV373471 (20020418)
PAGES: 131 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: C07K-016/00A
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW ; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

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? s (cd8)(10n)(antibod? or immunoglobulin?) and (cd4)(10n)(antibod? or
immunoglobulin?) and 40(w)mg
          145743  CD8
         2126831  ANTIBOD?
          786284  IMMUNOGLOBULIN?
           14512  CD8(10N)(ANTIBOD? OR IMMUNOGLOBULIN?)
          238007  CD4
         2126831  ANTIBOD?
          786284  IMMUNOGLOBULIN?
           26137  CD4(10N)(ANTIBOD? OR IMMUNOGLOBULIN?)
         1345499  40
         1755168  MG
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          59773  40(W)MG
      S8     14  (CD8)(10N)(ANTIBOD? OR IMMUNOGLOBULIN?) AND
                 (CD4)(10N)(ANTIBOD? OR IMMUNOGLOBULIN?) AND 40(W)MG
? rd s8
      S9      8  RD S8  (unique items)
? t s9/3/all
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s19/7/8,22,60,65,78,84,91

19/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013502041 BIOSIS NO.: 200200095552
CD40-CD154 pathway blockade requires host macrophages to induce humoral unresponsiveness to pig hematopoietic cells in baboons
AUTHOR: Buhler L; Alwayn I P J; Basker M; Oravec G; Thall A; White-Scharf M E; Sachs D H; Awwad M; Cooper D K C (Reprint)
AUTHOR ADDRESS: Transplantation Biology Research Center, Massachusetts General Hospital, 13th Street, MGH East, Building 149-9019, Boston, MA, 02129, USA**USA
JOURNAL: Transplantation (Baltimore) 72 (11): p1759-1768 December 15, 2001 2001
MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The effect of CD154 blockade and macrophage depletion or inhibition on baboon humoral and cellular immune responses to pig antigens was studied in a pig-to-baboon peripheral blood mobilized progenitor cell (PBPC) transplantation model aimed at inducing ***tolerance*** . We infused pig PBPCs in baboons pretreated with a nonmyeloablative regimen along with routine anti-human CD154 monoclonal ***antibody*** (mAb) and macrophage-depleting or -inhibiting agents. Group 1 baboons (n=2) underwent a nonmyeloablative regimen and immunoadsorption of anti-Galalpha1,3Gal (Gal) antibody (Ab) before intravenous infusion of ***high*** ***doses*** (1.3-4.6X1010cells/kg) of PBPCs. In group 2 (n=5), cyclosporine was replaced by 8 ***doses*** of anti-CD154 mAb over 14 days. Group 3 (n=3) received the group 2 regimen plus medronate liposomes (n=2) or commercially available human intravenous immunoglobulin G depleted of anti-Gal Ab (n=1) to deplete/inhibit recipient macrophages. Group 1 developed sensitization to Gal and also developed new Ab to non-Gal porcine antigens within 10 to 20 days. In group 2, no sensitization to Gal or non-Gal determinants was seen, but Gal-reactive antibodies did return to their preleukocyte transplantation levels. CD154 blockade, therefore, induced humoral unresponsiveness to pig cells. In group 3, sensitization to Gal was seen in all three baboons at 20 days, and Abs against new porcine determinants developed in one baboon. The depletion or inhibition of host macrophages, therefore, prevented the induction of humoral unresponsiveness by CD154 blockade. These results suggest that CD154 blockade induces humoral unresponsiveness by a mechanism that involves the indirect pathway of antigen presentation. In vitro investigation of baboon anti-pig mixed lymphocyte reaction confirmed that only the indirect pathway is efficiently blocked by anti-CD154 mAb. The mechanism in which blockade of the CD40-CD154 pathway induces its effect remains to be determined, but it could involve the generation of regulatory cells capable of suppressing the direct pathway.

19/7/22 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012499955 BIOSIS NO.: 200000218268
Virus-induced abrogation of transplantation tolerance induced by donor-specific transfusion and anti-CD154 antibody

AUTHOR: Welsh Raymond M; Markees Thomas G; Woda Bruce A; Daniels Keith A; Brehm Michael A; Mordes John P; Greiner Dale L; Rossini Aldo A (Reprint)
AUTHOR ADDRESS: Diabetes Division, University of Massachusetts Medical School, 373 Plantation St., Two Biotech, Suite 218, Worcester, MA, 01605, USA**USA
JOURNAL: Journal of Virology 74 (5): p2210-2218 March, 2000 2000
MEDIUM: print
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Treatment with a 2-week course of anti-CD154 antibody and a single transfusion of donor leukocytes (a donor-specific transfusion or DST) permits skin allografts to survive for > 100 days in thymectomized mice. As clinical trials of this methodology in humans are contemplated, concern has been expressed that viral infection of graft recipients may disrupt ***tolerance*** to the allograft. We report that acute infection with lymphocytic choriomeningitis virus (LCMV) induced allograft rejection in mice treated with DST and anti-CD154 ***antibody*** if inoculated shortly after ***transplantation*** . Isografts resisted LCMV-induced rejection, and the interferon-inducing agent polyinosinic:polycytidylic acid did not induce allograft rejection, suggesting that the effect of LCMV is not simply a consequence of nonspecific inflammation. Administration of anti-CD8 ***antibody*** to engrafted mice delayed LCMV-induced allograft rejection. Pichinde virus also induced acute allograft rejection, but murine cytomegalovirus and vaccinia virus (VV) did not. Injection of LCMV apprx50 days after tolerance induction and transplantation had minimal effect on subsequent allograft survival. Treatment with DST and anti-CD154 antibody did not interfere with clearance of LCMV, but a normally nonlethal high dose of VV during tolerance induction and ***transplantation*** killed ***graft*** recipients. We conclude that DST and anti-CD154 antibody induce a tolerant state that can be broken shortly after ***transplantation*** by certain viral infections. Clinical application of transplantation tolerance protocols may require patient isolation to facilitate the procedure and to protect recipients.

19/7/60 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

06719409 EMBASE No: 1997000867
The dose-related effect of monoclonal antibodies against adhesion molecules ICAM-1 and LFA-1 on peripheral nerve allograft rejection in a rat model
Hertl M.C.; Strasberg S.R.; Mackinnon S.E.; Mohanakumar T.; Hunter D.A.; Nyack L.M.; Miyasaka M.
S.E. Mackinnon, Department of Surgery, Washington University School of Medicine, St. Louis, MO 63110 United States
Restorative Neurology and Neuroscience (RESTOR. NEUROL. NEUROSCI.) (Ireland) 1996, 10/3 (147-159)
CODEN: RNNEE ISSN: 0922-6028
PUBLISHER ITEM IDENTIFIER: S092260289600358X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Donor-specific immunosuppression using anti-intercellular adhesion molecule-1 (ICAM-1) and anti-lymphocyte function-associated antigen-1 (LFA-1) has been shown to inhibit nerve allograft rejection without side

effects. This ***dose*** -response study evaluated several ***dosing*** regimens using a 2-week course of three monoclonal antibodies (mAbs) against ICAM-1 and LFA-1 in combination on peripheral nerve allograft rejection in a rat model. Assessments of regeneration included walking track, electrophysiological, and histomorphologic analyses. Donor (ACI)-specific ***tolerance*** induction was assessed. Toxicity and mAb serum levels were monitored. At 18 weeks postengraftment, intermediate and high-dose groups were histologically indistinguishable from isograft controls, and superior to the untreated allograft group which demonstrated a significantly lower percent nerve tissue than all other groups. There were no differences in print length factor after 12 weeks or conduction velocity at sacrifice between any groups. ***Tolerance*** induction was not demonstrated. During mAb administration, animals in higher dose groups experienced temporary systemic side effects. This study demonstrated that a short course of mAb therapy directed against ICAM-1/LFA-1 inhibits rejection in rat peripheral nerve allografts by an unknown mechanism. The use of immune modulation in nerve transplantation may eliminate the need for systemic immunosuppression.

19/7/65 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE

06313670 EMBASE No: 1995351540
T-cell regulation
Choy E.H.S.; Kingsley G.H.; Panayi G.S.
UMDS, Rheumatology Unit, Guy's Hospital, St Thomas Street,London SE1 9RT United Kingdom
Bailliere's Clinical Rheumatology (BAILLIERE'S CLIN. RHEUMATOL.) (United Kingdom) 1995, 9/4 (653-671)
CODEN: BCRHE ISSN: 0950-3579
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

There is considerable evidence to implicate T cells in the pathogenesis of rheumatoid arthritis (RA). They initiate and sustain inflammation and therefore are attractive targets for immunotherapy. Several strategies targeting T cells have been tried in RA. The use of monoclonal antibodies to deplete T cells has been used extensively but with little success. Studies have shown that T cell depleting ***antibodies*** produce profound peripheral blood lymphopenia but they are less effective in depleting lymphocytes in the joint. Since clinical efficacy is likely to depend on depleting almost all synovial lymphocytes, high doses of monoclonal ***antibodies*** would have to be given. However, the invariably severe peripheral blood lymphopenia induced by such a regimen is likely to result in profound immunosuppression. Therefore, this strategy has been abandoned and recent attempts have been made to induce ***tolerance*** in RA. In animal models of RA, treatment with ***high*** dose non-depleting anti-CD4 monoclonal antibody protects them from arthritis induced by injection of streptococcal cell wall. In addition, it leads to a state of anergy which protects the animals from arthritis induction without further treatment with anti-CD4 monoclonal ***antibody*** . This is currently being used in clinical trials of RA. Other tolerance inducing treatment strategies include T cell or T cell receptor vaccination and oral ***tolerance*** . The former is particularly difficult since the rheumatoid arthritogenic antigen and the pathogenic T cell remain unknown. The latter has shown promise in placebo controlled trials although the ideal dosage remains unknown. The mechanism of action of oral tolerance involves either immunosuppressive T cell cytokines, T cell anergy or depletion.

19/7/78 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12685006 PMID: 10773997
Prope tolerance with induction using Campath 1H and low-dose cyclosporin monotherapy in 31 cadaveric renal allograft recipients.
Calne R; Moffatt S D; Friend P J; Jamieson N V; Bradley J A; Hale G; Firth J; Bradley J; Smith K G; Waldmann H
Department of Surgery, Addenbrooke's Hospital, UK.
Nippon Geka Gakkai zasshi (JAPAN) Mar 2000, 101 (3) p301-6, ISSN 0301-4894--Print Journal Code: 0405405
Publishing Model Print
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The last 40 years has been a period of remarkable evolution of organ transplantation from nothing to a well-established form of treatment with good short-term and tolerable long-term results. Nevertheless by ten years approximately 50% of grafts will have been lost due, mainly, to chronic rejection or the side-effects of immunosuppressive therapy. We now have a number of extremely powerful immunosuppressive drugs and antibodies with different mechanisms of action and the stage is set for a move from current continuous high dose immunosuppressive maintenance therapy to low ***dose*** or no maintenance immunosuppression. True tolerance can occur in man, examples being successful bone marrow transplantation and patients with liver grafts who have stopped immunosuppression after years of good function. The ***antibody*** Campath 1H with a unique target CH52 on T & B lymphocytes and monocytes has been used to eliminate lymphocytes from the blood for a month in patients with renal allografts who have then been maintained on half dose Cyclosporin without any other maintenance drug. The results with a mean two year follow-up have been encouraging, 29 patients having good function without receiving maintenance steroids. It is likely that this protocol could be improved since dosage timing and various minimal maintenance immunosuppressive protocols have not been fully investigated. This almost or "Prope" tolerance could be a major step forward providing a better quality of life for patients and inexpensive maintenance immunosuppression.
Record Date Created: 20000613
Record Date Completed: 20000613

19/7/84 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11931005 PMID: 9760577
Tolerance induction with CD4 monoclonal antibodies.
Waldmann H; Bemelman F; Cobbold S
Sir William Dunn School of Pathology, Oxford, UK.
Novartis Foundation symposium (ENGLAND) 1998, 215 p146-52; discussion 152-8, 186-90, ISSN 1528-2511--Print Journal Code: 9807767
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
One of the major goals of therapeutic immunosuppression is to be able to use short-term therapy to achieve long-term ***tolerance*** . Short courses of CD4 antibodies are able to create peripheral tolerance in a

mature immune system. The resulting ***tolerant*** state shows evidence of being dominant in that one can observe the features of linked suppression, transferable suppression and infectious tolerance in a variety of model systems. Only in the situation of administration of ***high*** doses of marrow could one find evidence of central and peripheral tolerance which had all the features of being deletional rather than regulatory. These findings suggest that attaining dominant ***tolerance*** and linked suppression may be the least invasive of all tolerance -inducing strategies for clinical application. (22 Refs.)
Record Date Created: 19981125
Record Date Completed: 19981125

19/7/91 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10728114 PMID: 8591647
Innovative treatment approaches for rheumatoid arthritis. T-cell regulation.
Choy E H; Kingsley G H; Panayi G S
UMDS, Rheumatology Unit, Guy's Hospital, London, UK.
Bailliere's clinical rheumatology (ENGLAND) Nov 1995, 9 (4) p653-71, ISSN 0950-3579--Print Journal Code: 8805770
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
There is considerable evidence to implicate T cells in the pathogenesis of rheumatoid arthritis (RA). They initiate and sustain inflammation and therefore are attractive targets for immunotherapy. Several strategies targeting T cells have been tried in RA. The use of monoclonal antibodies to deplete T cells have been used extensively but with little success. Studies have shown that T cell depleting ***antibodies*** produce profound peripheral blood lymphopenia but they are less effective in depleting lymphocytes in the joint. Since clinical efficacy is likely to depend on depleting almost all synovial lymphocytes, high doses of monoclonal ***antibodies*** would have to be given. However, the invariably severe peripheral blood lymphopenia induced by such a regimen is likely to result in profound immunosuppression. Therefore, this strategy has been abandoned and recent attempts have been made to induce ***tolerance*** in RA. In animal models of RA, treatment with ***high*** dose non-depleting anti-CD4 monoclonal antibody protects them from arthritis induced by injection of streptococcal cell wall. In addition, it leads to a state of anergy which protects the animals from arthritis induction without further treatment with anti-CD4 monoclonal ***antibody*** . This is currently being used in clinical trials of RA. Other tolerance inducing treatment strategies include T cell or T cell receptor vaccination and oral ***tolerance*** . The former is particularly difficult since the rheumatoid arthritogenic antigen and the pathogenic T cell remain unknown. The latter has shown promise in placebo controlled trials although the ideal dosage remains unknown. The mechanism of action of oral tolerance involves either immunosuppressive T cell cytokines, T cell anergy or depletion. (76 Refs.)
Record Date Created: 19960401
Record Date Completed: 19960401
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     $0.41  Estimated cost File1
     $0.41  Estimated cost this search
     $0.41  Estimated total session cost   0.116 DialUnits

File 410:Dialog Comm.-of-Interest Newsl/Jul (c) 2006 Dialog

      Set  Items  Description
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? set hi ;set hi
HILIGHT set on as ''
HILIGHT set on as ''
? begin 5,73,155,399
       25sep06 08:13:50 User208760 Session D2783.2
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     $0.00  Estimated cost File410
     $0.05  TELNET
     $0.05  Estimated cost this search
     $0.46  Estimated total session cost   0.216 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R) 1969-2006/Sep W3
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  File  73:EMBASE 1974-2006/Sep 25
         (c) 2006 Elsevier B.V.
  File 155:MEDLINE(R) 1950-2006/Sep 25
         (c) format only 2006 Dialog
  File 399:CA SEARCH(R) 1967-2006/UD=14514
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*File 399: Use is subject to the terms of your user/customer agreement.
IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.

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         2290814  BETA
           11429  GALACTOSIDE
         2605909  BINDING
         5980867  PROTEIN
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? s s1 and toleran?
            407  S1
         468910  TOLERAN?
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? rd s2
      S3       3  RD S2  (unique items)
? t s3/3/all

 3/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0013809032   BIOSIS NO.: 200200402543
Induction of allogenic T-cell hyporesponsiveness by galectin-1-mediated
  apoptotic and non-apoptotic mechanisms
AUTHOR: Rabinovich G A (Reprint); Ramhorst R E; Rubinstein N; Corigliano A;
  Daroqui M C; Kier-Joffe E B; Fainboim L
AUTHOR ADDRESS: Division de Inmunogenetica, Hospital de Clinicas' Jose de
  San Martin'. Facultad de Medicina, Universidad de Buenos Aires, Cordoba
```

2351, 3er Piso, 1120, Buenos Aires, Argentina**Argentina
JOURNAL: Cell Death and Differentiation 9 (6): p661-670 June, 2002 2002
MEDIUM: print
ISSN: 1350-9047
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/2 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12412421 EMBASE No: 2003517278
CD29 and CD7 Mediate Galectin-3-Induced Type II T-Cell Apoptosis
Fukumori T.; Takenaka Y.; Yoshii T.; Kim H.-R.C.; Hogan V.; Inohara H.; Kagawa S.; Raz A.
A. Raz, Tum. Progression/Metastasis Program, Karmanos Cancer Institute, 110 East Warren Avenue, Detroit, MI 48201 United States
AUTHOR EMAIL: raza@karmanos.org
Cancer Research (CANCER RES.) (United States) 01 DEC 2003, 63/23 (8302-8311)
CODEN: CNREA ISSN: 0008-5472
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 69

3/3/3 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12950426 PMID: 11097206
"Galectin-1 induces central and peripheral cell death: implications in T-cell physiopathology".
Sotomayor C E; Rabinovich G A
Dpto. Bioquimica Clinica Facultad de Ciencias Quimicas, Universidad Nacional de Cordoba, Argentina. csotomay@bioclin.fcq.unc.edu.ar
Developmental immunology (ENGLAND) 2000, 7 (2-4) p117-29, ISSN 1044-6672--Print Journal Code: 9200624
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
? t s3/7/all

3/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013809032 BIOSIS NO.: 200200402543
Induction of allogenic T-cell hyporesponsiveness by galectin-1-mediated apoptotic and non-apoptotic mechanisms
AUTHOR: Rabinovich G A (Reprint); Ramhorst R E; Rubinstein N; Corigliano A; Daroqui M C; Kier-Joffe E B; Fainboim L
AUTHOR ADDRESS: Division de Inmunogenetica, Hospital de Clinicas' Jose de San Martin'. Facultad de Medicina, Universidad de Buenos Aires, Cordoba 2351, 3er Piso, 1120, Buenos Aires, Argentina**Argentina
JOURNAL: Cell Death and Differentiation 9 (6): p661-670 June, 2002 2002
MEDIUM: print
ISSN: 1350-9047

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Galectin-1, a beta-galactoside-binding protein expressed at sites of T-cell activation and immune privilege, has shown specific immunosuppressive properties. Because of the implications of this protein in T-cell tolerance and its potential use to avoid graft rejection, we investigated the immunosuppressive effects of galectin-1 in the course of the human allogenic T-cell response. Galectin-1 induced a dose- and carbohydrate-dependent inhibition of the allogenic T-cell response. Addition of galectin-1 to alloreactive lymphocytes resulted in significant apoptosis of CD45RO-positive cells. This negative regulatory effect was accompanied by caspase activation, Bcl-2 downregulation and was prevented by addition of exogenous IL-2. In addition, a significant decrease of IFN-gamma production was detected in the non-apoptotic cell population, following exposure of alloreactive lymphocytes to galectin-1. Moreover, the immunosuppressive activity of this protein did not involve TGF-beta-mediated mechanisms. Since galectin-1 is expressed by activated T cells and could be acting by an autocrine negative loop to control human T-cell reactivity, we finally examined the regulated expression of this protein throughout the allogenic T-cell response. Expression of endogenous galectin-1 was detected at 24 h of cell culture, reaching its maximal levels after 72 h of allostimulation. The present study sets the basis for a potential use of galectin-1 as a selective immunosuppressive agent to limit T-cell-mediated reactivity during the effector phase of the alloimmune response.

3/7/2 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12412421 EMBASE No: 2003517278
CD29 and CD7 Mediate Galectin-3-Induced Type II T-Cell Apoptosis
Fukumori T.; Takenaka Y.; Yoshii T.; Kim H.-R.C.; Hogan V.; Inohara H.; Kagawa S.; Raz A.
A. Raz, Tum. Progression/Metastasis Program, Karmanos Cancer Institute, 110 East Warren Avenue, Detroit, MI 48201 United States
AUTHOR EMAIL: raza@karmanos.org
Cancer Research (CANCER RES.) (United States) 01 DEC 2003, 63/23 (8302-8311)
CODEN: CNREA ISSN: 0008-5472
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 69

Galectin (Gal)-3, a MSUBr 31,000 member of the beta - galactoside-binding protein family, is a multifunctional protein implicated in a variety of biological functions, including tumor cell adhesion, proliferation, differentiation, angiogenesis, apoptosis, cancer progression, and metastasis. Here, we report that secreted extracellular Gal-3 can signal apoptosis of human T leukemia cell lines, human peripheral blood mononuclear cells, and activated mouse T cells after binding to cell surface glycoconjugate receptors through carbohydrate-dependent interactions because the apoptotic effect was found to be inhibited by lactose, specific sugar inhibitor, and to be dose dependent. However, the apoptosis sensitivity to Gal-3 varied among the different cell lines tested. We report that Gal-3-null Jurkat, CEM, and MOLT-4 cells were significantly more sensitive to exogenous Gal-3 than SKW6.4 and H9 cells, which express Gal-3, suggesting a cross-talk between

the antiapoptotic activity of intracellular Gal-3 and proapoptotic activity of extracellular Gal-3. Furthermore, Gal-3-transfected CEM cells were found to be more resistant to CSUB2-ceramide-induced apoptosis than the control CEM cells. Identification of Gal-3 cell surface receptors revealed that Gal-3 binding to CD7 and CD29 (betaSUB1 integrin) induced apoptosis. Gal-3 binding to its cell surface receptors results in activation of mitochondrial apoptosis events including cytochrome c release and caspase-3 activation, but not caspase-8 activation. Taken together, these results suggest that the induction of T-cell apoptosis by secreted Gal-3 may play a role in the immune escape mechanism during tumor progression through the induction of apoptosis to cancer-infiltrating T cells. The induction of T-cell apoptosis by secreted Gal-3 is dependent in part on the presence or absence of cytoplasmic Gal-3, providing a new insight for the immune escape mechanism of cancer cells.

3/7/3 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12950426 PMID: 11097206
"Galectin-1 induces central and peripheral cell death: implications in T-cell physiopathology".
Sotomayor C E; Rabinovich G A
Dpto. Bioquimica Clinica Facultad de Ciencias Quimicas, Universidad Nacional de Cordoba, Argentina. csotomay@bioclin.fcq.unc.edu.ar
Developmental immunology (ENGLAND) 2000, 7 (2-4) p117-29, ISSN 1044-6672--Print Journal Code: 9200624
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The immune system has a remarkable capacity to maintain a state of equilibrium even as it responds to a diverse array of foreign proteins and despite its contact exposure to self-antigens. Apoptosis is one of the mechanisms aimed at preserving the homeostasis after the completion of an immune response, thus returning the immune system to a basal state and warranting the elimination of autoagressive cells in both central and peripheral lymphoid organs. Targeted deletions in critical genes involved in the apoptotic death machinery together with natural spontaneous mutations have clearly shown the importance of apoptosis in the regulation of the immune response. This complex scenario of stimulatory and inhibitory genes has been enriched with the finding that galectin-1, a 14.5 kDa beta-galactoside-binding protein, is able to induce apoptosis of immature cortical thymocytes and mature T cells by cross-linking cell surface glycoconjugates. Galectin-1 is present not only in central and peripheral lymphoid organs, but also at sites of immune privilege. In the present article we will discuss the implications of galectin-1-induced apoptosis in T-cell physiopathology in an attempt to validate its therapeutic potential in autoimmune and inflammatory diseases. (95 Refs.)
Record Date Created: 20010223
Record Date Completed: 20010301
? ds

Set	Items	Description
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S3	3	RD S2 (unique items)

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407 S1

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? rd s4
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? t s5/3/all

 5/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0014105038   BIOSIS NO.: 200300063757
Regulated expression and ultrastructural localization of galectin-1, a
  proapoptotic beta-galactoside-binding lectin, during spermatogenesis in
  rat testis.
AUTHOR: Dettin Luis; Rubinstein Natalia; Aoki Agustin; Rabinovich Gabriel A
  ; Maldonado Cristina A (Reprint)
AUTHOR ADDRESS: Centro de Microscopia Electronica, Facultad de Ciencias
  Medicas, Universidad Nacional de Cordoba, 5000, Casilla Postal 362,
  Cordoba, Argentina**Argentina
AUTHOR E-MAIL ADDRESS: cmaldon@cmefcm.uncor.edu
JOURNAL: Biology of Reproduction  68 (1): p51-59 January 2003 2003
MEDIUM: print
ISSN: 0006-3363
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English


 5/3/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0013809032   BIOSIS NO.: 200200402543
Induction of allogenic T-cell hyporesponsiveness by galectin-1-mediated
  apoptotic and non-apoptotic mechanisms
AUTHOR: Rabinovich G A (Reprint); Ramhorst R E; Rubinstein N; Corigliano A;
  Daroqui M C; Kier-Joffe E B; Fainboim L
AUTHOR ADDRESS: Division de Inmunogenetica, Hospital de Clinicas' Jose de
  San Martin'. Facultad de Medicina, Universidad de Buenos Aires, Cordoba
  2351, 3er Piso, 1120, Buenos Aires, Argentina**Argentina
JOURNAL: Cell Death and Differentiation  9 (6): p661-670 June, 2002 2002
MEDIUM: print
ISSN: 1350-9047
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English


 5/3/3     (Item 3 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0007282828   BIOSIS NO.: 199090067307
RECOMBINANT HUMAN BETA GALACTOSIDE BINDING LECTIN SUPPRESSES CLINICAL AND
  HISTOLOGICAL SIGNS OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS
AUTHOR: OFFNER H (Reprint); CELNIK B; BRINGMAN T S; CASENTINI-BOROCZ D;
  NEDWIN G E; VANDENBARK A A
AUTHOR ADDRESS: NEUROIMMUNOL RES 151D, VA MED CENT, PORTLAND, OREGON 97201,
  USA**USA
JOURNAL: Journal of Neuroimmunology  28 (2): p177-184 1990
ISSN: 0165-5728
DOCUMENT TYPE: Article
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RECORD TYPE: Abstract
LANGUAGE: ENGLISH
? t s5/7/3

5/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007282828 BIOSIS NO.: 199090067307
RECOMBINANT HUMAN BETA GALACTOSIDE BINDING LECTIN SUPPRESSES CLINICAL AND HISTOLOGICAL SIGNS OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS
AUTHOR: OFFNER H (Reprint); CELNIK B; BRINGMAN T S; CASENTINI-BOROCZ D; NEDWIN G E; VANDENBARK A A
AUTHOR ADDRESS: NEUROIMMUNOL RES 151D, VA MED CENT, PORTLAND, OREGON 97201, USA**USA
JOURNAL: Journal of Neuroimmunology 28 (2): p177-184 1990
ISSN: 0165-5728
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Human placental tissue contains regulatory molecules that may prevent allo-sensitization. Recently, a 14 kDa . ***beta*** .-galactoside binding protein with demonstrated immunoregulatory properties has been cloned using cDNA from human placenta and expressed in Escherichia coli. The present study assesses the ability of this recombinant immunomodulatory lectin (rIML-1), to prevent experimental autoimmune encephalomyelitis (EAE), a paralytic T cell-mediated disease directed against myelin basic protein (BP). Injection of rIML-1 into Lewis rats inhibited the induction of both clinical and histological signs of EAE, apparently by blocking sensitization of encephalitogenic BP-specific T cells and inducing BP-dependent suppressor cells. Because it is neither immunogenic not toxic, rIML-1 may have application in humans, and would have distinct advantages over unselective cytotoxic immunosuppressive agents used currently in the treatment of autoimmune diseases and transplantation.
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407 S1
967693 SUPPRESS?
4647620 INHIBIT?
645729 GRAFT?
1717002 TRANSPLANT?
48661 (SUPPRESS? OR INHIBIT?)(20N)(GRAFT? OR TRANSPLANT?)
S6 0 S1 AND (SUPPRESS? OR INHIBIT?)(20N)(GRAFT? OR TRANSPLANT?)
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Processing
Processing
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407 S1
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4647620 INHIBIT?
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728569 T(W)CELL?
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1332869 LYMPHOCYT?
499240 T(W)LYMPHOCYT?
0 CD4? RO CD8?

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                  T(W)LYMPHOCYT? OR CD4? RO CD8?)
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      S8       0  RD S7
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      S9      11  RD S7  (unique items)
? t s9/7/all

 9/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0015181545   BIOSIS NO.: 200500088610
Regulated expression of galectin-1 during T-cell activation involves Lck
  and Fyn kinases and signaling through MEK1/ERK, p38 MAP kinase and p70S6
  kinase
AUTHOR: Fuertes Mercedes B; Molinero Luciana L; Toscano Marta A; Ilarregui
  Juan M; Rubinstein Natalia; Fainboim Leonardo; Zwirner Norberto W;
  Rabinovich Gabriel A (Reprint)
AUTHOR ADDRESS: Fac MedHosp Clin Jose de San MartinDept Microbiol,Div
  Immunogenet, Univ Buenos Aires, Av Cordoba 2351,3er Piso C1120AAF, Buenos
  Aires, DF, Argentina**Argentina
AUTHOR E-MAIL ADDRESS: gabyrabi@ciudad.com.ar
JOURNAL: Molecular and Cellular Biochemistry  267 (1-2): p177-185 December
2004 2004
MEDIUM: print
ISSN: 0300-8177 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recent evidence has implicated galectins and their carbohydrate
  ligands as novel regulators of  ***T***  -  ***cell***  homeostasis. Galectin-1
  (Gal-1), a member of this family, inhibits clonal expansion,
  induces apoptosis of antigen-primed T lymphocytes and
  suppresses the development of T-cell-mediated
  autoimmune diseases in vivo. Because the  ***beta***  -  ***galactoside***  -
  binding protein is expressed in activated but not resting T
  cells, it has been hypothesized that Gal-1-induced apoptosis may
  constitute an autocrine suicide mechanism to eliminate activated T cells
  contributing to the termination of an effector immune response. We
  undertook this study to investigate the signals and intracellular
  pathways leading to Gal-1 expression during T-cell activation. When T
  cells were stimulated either with anti-CD3 or anti-CD28 monoclonal
  antibody plus PMA in the presence of accessory cells, a sustained
  up-regulation of Gal-1 was observed, reaching a plateau between days 3
  and 5 following CD3 engagement or costimulation through CD28.
  Investigation of the signal transduction events involved in this process
  revealed a role for Lck and Fyn kinases, since the Src kinase
  inhibitor PP1 inhibited the up-regulated expression of Gal-1
  following  ***T***  -  ***cell***  activation. Downstream signaling routes
  involve mitogen-activated protein kinase (MAPK) kinase
  (MEK)1/extracellular signal-regulated kinase (ERK) and p38 MAPK, as Gal-1
  expression was prevented by U0126 and SB202190. In addition, expression
  of Gal-1 involves interleukin(IL)-2-dependent signaling routes triggered
  by p70S6 kinase, as it could be inhibited by rapamycin. This is the first
  demonstration of the intracellular pathways that control
  activation-induced expression of Gal-1, which may reveal potential
  targets for immune intervention to modulate expression of this beta
  -  ***galactoside***  -  ***binding***  ***protein***  in pathological
disorders.
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9/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014669211 BIOSIS NO.: 200400039968
CD29 and CD7 mediate galectin-3-induced type II T-cell apoptosis.
AUTHOR: Fukumori Tomoharu; Takenaka Yukinori; Yoshii Tadashi; Kim Hyeong-Reh Choi; Hogan Victor; Inohara Hidenori; Kagawa Susumu; Raz Avraham (Reprint)
AUTHOR ADDRESS: Tumor Progression and Metastasis Program, Karmanos Cancer Institute, 110 East Warren Avenue, Detroit, MI, 48201, USA**USA
AUTHOR E-MAIL ADDRESS: raza@karmanos.org
JOURNAL: Cancer Research 63 (23): p8302-8311 December 1, 2003 2003
MEDIUM: print
ISSN: 0008-5472 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Galectin (Gal)-3, a Mr 31,000 member of the beta-galactoside-binding protein family, is a multifunctional protein implicated in a variety of biological functions, including tumor cell adhesion, proliferation, differentiation, angiogenesis, apoptosis, cancer progression, and metastasis. Here, we report that secreted extracellular Gal-3 can signal apoptosis of human T leukemia cell lines, human peripheral blood mononuclear cells, and activated mouse T cells after binding to cell surface glycoconjugate receptors through carbohydrate-dependent interactions because the apoptotic effect was found to be inhibited by lactose, specific sugar inhibitor, and to be dose dependent. However, the apoptosis sensitivity to Gal-3 varied among the different cell lines tested. We report that Gal-3-null Jurkat, CEM, and MOLT-4 cells were significantly more sensitive to exogenous Gal-3 than SKW6.4 and H9 cells, which express Gal-3, suggesting a cross-talk between the antiapoptotic activity of intracellular Gal-3 and proapoptotic activity of extracellular Gal-3. Furthermore, Gal-3-transfected CEM cells were found to be more resistant to C2-ceramide-induced apoptosis than the control CEM cells. Identification of Gal-3 cell surface receptors revealed that Gal-3 binding to CD7 and CD29 (beta1 integrin) induced apoptosis. Gal-3 binding to its cell surface receptors results in activation of mitochondrial apoptosis events including cytochrome c release and caspase-3 activation, but not caspase-8 activation. Taken together, these results suggest that the induction of T-cell apoptosis by secreted Gal-3 may play a role in the immune escape mechanism during tumor progression through the induction of apoptosis to cancer-infiltrating T cells. The induction of T-cell apoptosis by secreted Gal-3 is dependent in part on the presence or absence of cytoplasmic Gal-3, providing a new insight for the immune escape mechanism of cancer cells.

9/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014105038 BIOSIS NO.: 200300063757
Regulated expression and ultrastructural localization of galectin-1, a proapoptotic beta-galactoside-binding lectin, during spermatogenesis in rat testis.
AUTHOR: Dettin Luis; Rubinstein Natalia; Aoki Agustin; Rabinovich Gabriel A ; Maldonado Cristina A (Reprint)

AUTHOR ADDRESS: Centro de Microscopia Electronica, Facultad de Ciencias Medicas, Universidad Nacional de Cordoba, 5000, Casilla Postal 362, Cordoba, Argentina**Argentina
AUTHOR E-MAIL ADDRESS: cmaldon@cmefcm.uncor.edu
JOURNAL: Biology of Reproduction 68 (1): p51-59 January 2003 2003
MEDIUM: print
ISSN: 0006-3363
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Galectin-1, a highly conserved beta-galactoside-binding protein, induces apoptosis of activated T cells and suppresses the development of autoimmunity and chronic inflammation. To gain insight regarding the potential role of galectin-1 as a novel mechanism of immune privilege, we investigated expression and ultrastructural localization of galectin-1 in rat testis. Galectin-1 expression was assessed by Western blot analysis and immunocytochemical localization in testes obtained from rats aged from 9 to 60 days. Expression of this carbohydrate-binding protein was developmentally regulated, and its immunolabeling exhibited a stage-specific pattern throughout the spermatogenic process. Immunogold staining using the anti-galectin-1 antibody revealed the typical Sertoli cell profile in the seminiferous epithelium, mainly at stages X-II. During spermiation (stages VI-VIII), a strong labeling was observed at the luminal pole of seminiferous epithelium, localized on apical stalks of Sertoli cells, on heads of mature spermatids, and on bodies of residual cytoplasm. Moreover, spermatozoa released into the lumen showed a strong immunostaining. Following spermiation (stage VIII), galectin-1 expression was restored at the basal portion of Sertoli cells and progressively spread out through the whole cells as differentiation of germinal cells proceeded. Immunoelectron microscopy confirmed distribution of galectin-1 in nuclei and cytoplasmic projections of Sertoli cells and on heads and tails of late spermatids and residual bodies. Surface localization of galectin-1 was evidenced in spermatozoa from caput epididymis. Thus, the regulated expression of galectin-1 during the spermatogenic cycle suggests a novel role for this immunosuppressive lectin in reproductive biology.

9/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013809032 BIOSIS NO.: 200200402543
Induction of allogenic T-cell hyporesponsiveness by galectin-1-mediated apoptotic and non-apoptotic mechanisms
AUTHOR: Rabinovich G A (Reprint); Ramhorst R E; Rubinstein N; Corigliano A; Daroqui M C; Kier-Joffe E B; Fainboim L
AUTHOR ADDRESS: Division de Inmunogenetica, Hospital de Clinicas' Jose de San Martin'. Facultad de Medicina, Universidad de Buenos Aires, Cordoba 2351, 3er Piso, 1120, Buenos Aires, Argentina**Argentina
JOURNAL: Cell Death and Differentiation 9 (6): p661-670 June, 2002 2002
MEDIUM: print
ISSN: 1350-9047
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Galectin-1, a beta-galactoside-binding protein expressed at sites of T-cell activation and immune privilege, has shown specific immunosuppressive properties. Because of

the implications of this protein in T-cell tolerance and its potential use to avoid graft rejection, we investigated the immunosuppressive effects of galectin-1 in the course of the human allogenic T-***cell*** response. Galectin-1 induced a dose- and carbohydrate-dependent inhibition of the allogenic T-***cell*** response. Addition of galectin-1 to alloreactive lymphocytes resulted in significant apoptosis of CD45RO-positive cells. This negative regulatory effect was accompanied by caspase activation, Bcl-2 downregulation and was prevented by addition of exogenous IL-2. In addition, a significant decrease of IFN-gamma production was detected in the non-apoptotic cell population, following exposure of alloreactive lymphocytes to galectin-1. Moreover, the immunosuppressive activity of this protein did not involve TGF-beta-mediated mechanisms. Since galectin-1 is expressed by activated T cells and could be acting by an autocrine negative loop to control human T-cell reactivity, we finally examined the regulated expression of this protein throughout the allogenic T-cell response. Expression of endogenous galectin-1 was detected at 24 h of cell culture, reaching its maximal levels after 72 h of allostimulation. The present study sets the basis for a potential use of galectin-1 as a selective immunosuppressive agent to limit T-cell-mediated reactivity during the effector phase of the alloimmune response.

9/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013049139 BIOSIS NO.: 200100220978
Expression and function of galectin-3, a beta-galactoside-binding protein in activated T lymphocytes
AUTHOR: Joo Hong-Gu; Goedegebuure Peter S (Reprint); Sadanaga Noriaki; Nagoshi Makoto; von Bernstorff Wolfram; Eberlein Timothy J
AUTHOR ADDRESS: Department of Surgery, Washington University School of Medicine, 660 S. Euclid Ave., Saint Louis, MO, 63110, USA**USA
JOURNAL: Journal of Leukocyte Biology 69 (4): p555-564 April, 2001 2001
MEDIUM: print
ISSN: 0741-5400
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A soluble beta-galactoside-binding lectin, galectin-3 has been shown to be involved in cell adhesion and activation of immune cells. Although galectin-3 is known to be expressed in various types of cells, it has not been shown whether galectin-3 is expressed in T lymphocytes. We present evidence here that galectin-3 is expressed in activated murine T lymphocytes including CD4+ and CD8+ T cells but not in resting T cells. Galectin-3 expression was induced by anti-CD3 mAb or mitogen and enhanced by common gamma-chain signaling cytokines, IL-2, IL-4, and IL-7, in activated T lymphocytes, whereas the inflammatory cytokines including TNF-alpha and IFN-gamma did not. Galectin-3 expression and proliferation were down-regulated by withdrawal of IL-2 and gamma irradiation. Anti-sense but not sense phosphorothioated oligonucleotides for galectin-3 inhibited galectin-3 expression and blocked proliferation of ***T*** ***cells*** significantly. This study suggests that up-regulation of galectin-3 plays an important role in proliferation of activated T lymphocytes.

9/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011639824 BIOSIS NO.: 199800434071
beta-galactoside-binding protein secreted by activated T cells inhibit antigen-induced proliferations of T cells
AUTHOR: Blaser Claudine; Kaufmann Martin; Mueller Christoph; Zimmermann Christine; Wells Valerie; Mallucci Livio; Pirche Hanspeter (Reprint)
AUTHOR ADDRESS: Inst. Med. Microbiol. Hygiene, Dep. Immunol., Hermann-Herder-Str. 11, Univ. Freiburg, D-79104 Freiburg, Germany** Germany
JOURNAL: European Journal of Immunology 28 (8): p2311-2319 Aug., 1998 1998
MEDIUM: print
ISSN: 0014-2980
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have used mRNA differential display PCR to search for genes induced in activated T cells and have found the LGALS1 (lectin, galactoside-binding, soluble) gene to be strongly upregulated in effector T cells. The protein coded by the LGALS1 gene is a ***beta*** - galactoside-binding protein (betaGBP), which is released by cells as a monomeric negative growth factor but which can also associate into homodimers (galectin-1) with lectin properties. Northern blot analysis revealed that ex vivo isolated CD8+ effector T cells induced by a viral infection expressed high amounts of LGALS1 mRNA, whereas LGALS1 expression was almost absent in resting CD8+ T cells. LGALS1 expression could be induced in CD4+ and CD8+ T cells upon activation with the cognate peptide antigen and high levels of LGALS1 expression were found in concanavalin A-activated T cells but not in lipopolysaccharide-activated B cells. Gel filtration and Western blot analysis revealed that only monomeric betaGBP was released by activated CD8+ T cells and in vitro experiments further showed that recombinant betaGBP was able to inhibit antigen-induced proliferation of naive and antigen-experienced CD8+ ***T*** ***cells*** . Thus, these data indicate a role of betaGBP as an autocrine negative growth factor for CD8+ T cells.

9/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007282828 BIOSIS NO.: 199090067307
RECOMBINANT HUMAN BETA GALACTOSIDE BINDING LECTIN SUPPRESSES CLINICAL AND HISTOLOGICAL SIGNS OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS
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LANGUAGE: ENGLISH

ABSTRACT: Human placental tissue contains regulatory molecules that may prevent allo-sensitization. Recently, a 14 kDa . ***beta*** .- galactoside binding protein with demonstrated immunoregulatory properties has been cloned using cDNA from human placenta and expressed in Escherichia coli. The present study assesses

the ability of this recombinant immunomodulatory lectin (rIML-1), to prevent experimental autoimmune encephalomyelitis (EAE), a paralytic T cell-mediated disease directed against myelin basic protein (BP). Injection of rIML-1 into Lewis rats inhibited the induction of both clinical and histological signs of EAE, apparently by blocking sensitization of encephalitogenic BP-specific T cells and inducing BP-dependent ***suppressor*** cells. Because it is neither immunogenic not toxic, rIML-1 may have application in humans, and would have distinct advantages over unselective cytotoxic immunosuppressive agents used currently in the treatment of autoimmune diseases and transplantation.

9/7/8 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12906013 EMBASE No: 2004509177

Regulated expression of galectin-1 during T-cell activation involves Lck and Fyn kinases and signaling through MEK1/ERK, p38 MAP kinase and p70SUPS6 kinase

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LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 58

Recent evidence has implicated galectins and their carbohydrate ligands as novel regulators of ***T*** - ***cell*** homeostasis. Galectin-1 (Gal-1), a member of this family, inhibits clonal expansion, induces apoptosis of antigen-primed T lymphocytes and suppresses the development of ***T*** - ***cell*** -mediated autoimmune diseases in vivo. Because the beta-galactoside-binding protein is expressed in activated but not resting T cells, it has been hypothesized that Gal-1-induced apoptosis may constitute an autocrine suicide mechanism to eliminate activated T-cells contributing to the termination of an effector immune response. We undertook this study to investigate the signals and intracellular pathways leading to Gal-1 expression during T-cell activation. When T cells were stimulated either with anti-CD3 or anti-CD28 monoclonal antibody plus PMA in the presence of accessory cells, a sustained up-regulation of Gal-1 was observed, reaching a plateau between days 3 and 5 following CD3 engagement or costimulation through CD28. Investigation of the signal transduction events involved in this process revealed a role for Lck and Fyn kinases, since the Src kinase inhibitor PP1 inhibited the up-regulated expression of Gal-1 following ***T*** - ***cell*** activation. Downstream signaling routes involve mitogen-activated protein kinase (MAPK) kinase (MEK)1/extracellular signal-regulated kinase (ERK) and p38 MAPK, as Gal-1 expression was prevented by U0126 and SB202190. In addition, expression of Gal-1 involves interleukin (IL)-2-dependent signaling routes triggered by p70SUPS6 kinase, as it could be inhibited by rapamycin. This is the first demonstration of the intracellular pathways that control activation-induced expression of Gal-1, which may reveal potential targets for immune intervention to modulate expression of this beta-galactoside-binding ***protein*** in pathological disorders. (c) 2004 Kluwer Academic Publishers.

9/7/9 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11620182 EMBASE No: 2002192325
Functional analysis of the carbohydrate recognition domains and a linker peptide of galectin-9 as to eosinophil chemoattractant activity
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Glycobiology (GLYCOBIOLOGY) (United Kingdom) 2002, 12/3 (191-197)
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NUMBER OF REFERENCES: 18

Human galectin-9 is a beta-galactoside-binding protein consisting of two carbohydrate recognition domains (CRDs) and a linker peptide. We have shown that galectin-9 represents a novel class of eosinophil chemoattractants (ECAs) produced by activated T cells. A previous study demonstrated that the carbohydrate binding activity of galectin-9 is indispensable for eosinophil chemoattraction and that the N- and C-terminal CRDs exhibit comparable ECA activity, which is substantially lower than that of full-length galectin-9. In this study, we investigated the roles of the two CRDs in ECA activity in conjunction with the sugar-binding properties of the CRDs. In addition, to address the significance of the linker peptide structure, we compare the three isoforms of galectin-9, which only differ in the linker peptide region, in terms of ECA activity. Recombinant proteins consisting of two N-terminal CRDs (galectin-9NN), two C-terminal CRDs (galectin-9CC), and three isoforms of galectin-9 (galectin-9S, -9M, and -9L) were generated. All the recombinant proteins had hemagglutination activity comparable to that of the predominant wild-type galectin-9 (galectin-9M). Galectin-9NN and galectin-9CC induced eosinophil chemotaxis in a manner indistinguishable from the case of galectin-9M. Although the isoform of galectin-9 with the longest linker peptide, galectin-9L, exhibited limited solubility, the three isoforms showed comparable ECA activity over the concentration range tested. The interactions between N- and C-terminal CRDs and glycoprotein glycans and glycolipid glycans were examined using frontal affinity chromatography. Both CRDs exhibited high affinity for branched complex type sugar chain, especially for tri- and tetraantennary N-linked glycans with N-acetyllactosamine units, and the oligosaccharides inhibited the ECA activity at low concentrations. These results suggest that the N- and C-terminal CRDs of galectin-9 interact with the same or a closely related ligand on the eosinophil membrane when acting as an ECA and that ECA activity does not depend on a specific structure of the linker peptide.

9/7/10 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

07381233 EMBASE No: 1998291146
beta-Galactoside-binding protein (betaGBP) alters the cell cycle, up- regulates expression of the alpha- and beta-chains of the IFN-gamma receptor, and triggers IFN-gamma-mediated apoptosis of activated human T lymphocytes
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NUMBER OF REFERENCES: 32

In this paper, the effects of beta-galactoside binding protein (betaGBP), the LGALS1 gene product, on the cell cycle progression and expansion of activated human T lymphocytes were studied. betaGBP drastically ***inhibits*** the IL-2 induced proliferation of PHA-activated T lymphocytes as well as the IL- 2 independent proliferation of malignant T lymphocytes by arresting them in the S and Ginf 2/M phases of the cell cycle. In addition, betaGBP up-regulates the expression of both the alpha- and the beta-chains of the IFN-gammaR on activated T lymphocyte membrane. None of these effects depend on sugar binding: saturating amounts of lactose do not affect the cell cycle block nor IFN-gammaR up-modulation. The increased expression of both chains renders betaGBP-treated T lymphoblasts sensitive to IFN-gamma-induced apoptosis. Taken as a whole, these findings suggest that betaGBP plays an important immunoregulatory role by switching off T lymphocyte effector functions. They also provide the first evidence of up-modulation of IFN-gammaR expression on T lymphocytes by a negative cell growth regulator.

9/7/11 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

06997992 EMBASE No: 1997284200
Specific inhibition of lymphocyte proliferation and induction of apoptosis by CLL-I, a beta-galactoside-binding lectin
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Journal of Biochemistry (J. BIOCHEM.) (Japan) 1997, 122/2 (365-373)
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NUMBER OF REFERENCES: 54

beta-Galactoside-binding lectins or galectins are a family of closely related carbohydrate binding proteins which functions still remain to be elucidated. Several evidence suggest they could play a role in different biological processes, such as cell growth regulation and immunomodulation. In the present study we report that affinity-purified CLL-I (chicken lactose lectin-I), an acidic 16-kDa galectin exhibits specific growth regulatory properties. Con A-stimulated rat spleen mononuclear cells showed a marked dose-dependent growth inhibition upon incubation with the galectin protein. Cell growth arrest was highly prevented by galectin-specific sugars. In addition, biochemical, cytofluorometrical, and morphological evidence are also provided to show that these inhibitory properties are related to a positive control in the apoptotic threshold of spleen mononuclear cells. Flow cytometric analysis showed a dose- and time-dependent increase of cells with hypodiploid DNA content upon exposure to CLL-I. Moreover, cells treated with CLL-I displayed the typical

ultrastructural changes compatible with apoptosis, mainly chromatin condensation and margination along the inner surface of the nuclear envelope. Finally, the highly characteristic 'ladder' pattern of DNA fragmentation into oligonucleosome-length fragments of ~ 180-200 bp could be found within 6 h of cell culture with CLL-I, mainly in the T cell-enriched population. Induction of apoptosis by a ***beta*** - galactoside-binding protein highlights a potentially novel mechanism for regulating the immune response and points to a rational basis for the postulated immunomodulatory properties of this protein family.
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